Journal of Food Innovation, Nutrition, and Environmental Sciences
September, 2026, Volume 3; Issue 3: 404–413
ISSN No: 3078-5537

CASE REPORT

Longitudinal Lipid Profile Variability Suggestive of a Lean Mass Hyper-Responder-like Pattern During Ketogenic Diet Adherence: A Case Report

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DOI: https://doi.org/10.70851/jfines.2026.3(3).404.413

ABSTRACT

The ketogenic diet (KD) is widely used for weight loss and metabolic health improvement, and some individuals experience substantial increases in low-density lipoprotein (LDL) cholesterol, a pattern recently described in the context of the lean mass hyper-responder (LMHR) phenotype. This case report describes longitudinal changes in lipid profile, liver function, and metabolic parameters over 28 months of follow-up in an adult without known cardiovascular, diabetic, renal, hepatic, or endocrine disease, adhering to a KD initiated in January 2024. No pre-diet lipid values were available. Five laboratory assessments performed between June 2024 and May 2026 were analyzed. Total cholesterol ranged from 194 to 382 mg/dL and LDL cholesterol from 137.4 to 295.8 mg/dL, reflecting marked intra-individual variability rather than persistent elevation. Triglycerides remained low (23–99 mg/dL) throughout follow-up, and HDL cholesterol remained within a generally favorable range (44–76.2 mg/dL) but never reached the ≥80 mg/dL threshold formally required for the LMHR phenotype. A transient elevation of alanine aminotransferase (ALT; 132 U/L) and aspartate aminotransferase (AST; 74 U/L) was observed in January 2026, with subsequent resolution. Nutritional ketosis was objectively confirmed via capillary β-hydroxybutyrate monitoring (range 0.5–2.3 mmol/L) three times weekly throughout follow-up. Several parameters (HbA1c, free thyroxine, free testosterone) were measured only once and should not be interpreted as longitudinally stable. Consequently, the lipid pattern observed—marked LDL-C variability with persistently low triglycerides and high-normal HDL-C—is best described as an LMHR-like pattern rather than a confirmed LMHR phenotype, highlighting the need for further research to clarify the clinical implications of extreme LDL fluctuations in adults without known metabolic disease who do not fully meet strict phenotypic criteria.

Article history
Received;
30 July, 2026
Revised;
19 August, 2026
Accepted;
01 September, 2026

Keywords
ketogenic diet
lean mass hyper-responder-like pattern
lipid profile
nutritional ketosis
case report

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Peer review under responsibility of Journal of Food Innovations, Nutrition, and Environmental Sciences

A Publication of EcoScribe Publishers company Limited, Uganda. www.ecoscribepublishers.com

1. INTRODUCTION

The ketogenic diet (KD) is a dietary pattern characterized by marked carbohydrate restriction, moderate protein intake, and high fat consumption, with the goal of inducing a physiological state known as nutritional ketosis. In this metabolic state, reduced glucose availability promotes increased fatty acid oxidation and hepatic production of ketone bodies—primarily β-hydroxybutyrate, acetoacetate, and acetone—which serve as alternative energy substrates for multiple tissues, including the central nervous system (Paoli, 2014; Daley et al., 2026). Initially developed as a treatment for refractory epilepsy in the 1920s, the KD has experienced renewed interest due to its potential application in body weight control, type 2 diabetes, metabolic syndrome, and other chronic conditions associated with insulin resistance (Neal et al., 2008; Westman et al., 2008). Several studies have shown that this nutritional approach can lead to significant reductions in body weight, fat mass, plasma triglycerides, and blood glucose, together with increases in high-density lipoprotein (HDL) cholesterol concentrations (Bueno et al., 2013; Mansoor et al., 2016; Choi et al., 2020). It should be noted that KDs and broader low-carbohydrate diets are not always equivalent interventions, and evidence obtained from one should not be uncritically extrapolated to the other.

However, the effects of the KD on the lipid profile remain a matter of debate. While most studies report decreases in triglycerides and improvements in certain cardiometabolic markers, the response of low-density lipoprotein (LDL) cholesterol appears highly variable between individuals (Santos et al., 2012). Some people show minimal changes or even reductions in LDL concentrations, whereas others experience marked increases that may substantially exceed levels considered optimal in current clinical guidelines (Norwitz et al., 2022b).

Recently, a particular metabolic phenotype termed the lean mass hyper-responder (LMHR) has been described, characterized by elevated LDL cholesterol (≥200 mg/dL), high HDL cholesterol (≥80 mg/dL), and low triglycerides (≤70 mg/dL) in metabolically healthy individuals following low-carbohydrate diets (Norwitz et al., 2022a). This pattern appears more frequent in lean, physically active individuals with high metabolic flexibility, suggesting underlying physiological mechanisms distinct from those observed in hypercholesterolemia associated with metabolic syndrome (Norwitz et al., 2022a; Cooper et al., 2023). These thresholds were deliberately selected as statistically rare in the general population, such that meeting all three simultaneously would be highly unlikely by chance alone; the strictness of this triad is therefore central to the definition of the phenotype, rather than an incidental feature.

The so-called lipid energy model proposes that, under significant carbohydrate restriction, the body increases the transport of triglycerides and cholesterol via very low-density lipoproteins (VLDL) to meet peripheral energy demands. As a consequence, circulating LDL particles derived from VLDL metabolism may increase, leading to substantial elevations in LDL cholesterol without concomitant deterioration in other metabolic indicators (Norwitz et al., 2022; Cooper et al., 2023; Feldman et al., 2022). Although this hypothesis has generated considerable scientific interest, current evidence remains limited and requires confirmation through longitudinal studies and controlled clinical trials.

The clinical interpretation of these LDL elevations represents one of the main challenges in research on low-carbohydrate diets. Cardiovascular prevention guidelines regard LDL cholesterol as a causal factor in atherosclerosis and recommend its reduction to decrease cardiovascular risk (Mach et al., 2020; ESC/EAS, 2025). Nonetheless, some researchers have suggested that the prognostic significance of LDL elevations observed in metabolically healthy individuals under nutritional ketosis may differ from that seen in contexts of insulin resistance, obesity, or chronic inflammation (Diamond & Leaverton, 2023). This controversy has stimulated growing interest in better understanding the metabolic adaptations associated with the KD and their potential long-term impact on cardiovascular health.

Beyond lipid changes, KDs have been associated with improved insulin sensitivity, reduced glycated hemoglobin, decreased C-reactive protein, and preserved renal function (Athinarayanan et al., 2019, 2025; García-Silva et al., 2024). Transient elevations in hepatic enzymes have occasionally been reported during metabolic adaptation, although the mechanisms remain poorly characterized and are likely multifactorial.

Most available evidence derives from population studies or short interventions; detailed longitudinal data in individuals with extreme lipid responses remain scarce. To our knowledge, this case is among the few reports combining objective ketone monitoring, body composition assessment, and detailed dietary quantification over more than two years of ketogenic-diet adherence, providing a more rigorous longitudinal characterization than previously published LMHR-like case reports. Therefore, the aim of this case report was to describe longitudinal changes in lipid profile, liver function, and metabolic parameters over 28 months of follow-up in an adult adhering to a KD, and to critically examine the extent to which the observed pattern corresponds to the formally defined LMHR phenotype.

2. MATERIALS AND METHODS

2.1 Study design

A longitudinal observational single-case study was conducted based on the retrospective analysis of routine clinical follow-up data from an adult who adhered to a KD initiated in January 2024, followed for 28 months. This design allowed the temporal evolution of hematological, metabolic, hormonal, dietary, and biochemical biomarkers to be evaluated through serial laboratory assessments and clinical evaluations performed during the follow-up period.

2.2 Participant

The study included a 34-year-old male without known history of cardiovascular disease, diabetes mellitus, chronic kidney disease, liver disease, or diagnosed endocrine disorders. Five laboratory assessments performed between June 2024 and May 2026, as part of his routine clinical follow-up, were analyzed. No lipid profile data prior to diet initiation (January 2024) were available; this absence of a true pre-diet baseline is acknowledged as a limitation.

2.2.1 Timeline of dietary and lifestyle intervention

The participant initiated a strict KD in January 2024 as a nutritional strategy aimed at improving body composition, metabolic health, and physical functionality. During the first phase of intervention, corresponding to approximately the first 12 months of follow-up, physical activity was limited primarily to low-intensity aerobic exercise, mainly regular walking. During this period, a progressive adaptation to nutritional ketosis occurred without clinically relevant adverse events or symptoms of metabolic intolerance.

In January 2025, after approximately 12 months of continuous adherence to the ketogenic pattern, the participant incorporated resistance training at a frequency of three sessions per week. Concurrently, he began daily supplementation with vitamin D (4,000 IU) and magnesium bisglycinate. Adequate tolerance to strength training was observed, with no functional limitations or clinical signs compatible with impaired physical performance related to carbohydrate restriction.

Six months later, approximately in July 2025 (18 months of follow-up), the participant added calisthenics exercises integrated within resistance training sessions, maintaining a weekly frequency of three training days. Simultaneously, he began supplementation with creatine monohydrate and omega-3 fatty acids, while continuing prior vitamin D and magnesium supplementation.

Between July 2025 and May 2026, the participant maintained both strict adherence to the KD and the combined resistance training/calisthenics program, without clinically relevant complications, symptoms of dehydration, functional deterioration, or signs suggestive of endocrine, renal, or hepatic alterations. Physical activity information throughout this period was obtained through patient self-report during routine clinical follow-up, without objective monitoring (e.g., accelerometry or heart rate tracking).

Finally, in May 2026, after a total of 28 months of follow-up, a comprehensive clinical evaluation was performed, including segmental multifrequency bioelectrical impedance analysis and a complete laboratory workup (**Figure 1**).

2.2.2 Dietary adherence

Dietary intake was recorded through daily weighing of all foods consumed in the single daily meal, using a precision kitchen scale, throughout the entire intervention period. Energy content and macronutrient composition (protein, fat, and carbohydrate) were estimated using the Spanish Food Composition Database (BEDCA) and, for nutrients not available in that database, the USDA FoodData Central, ensuring accurate and standardized daily quantification of caloric and macronutrient intake throughout the study period.

The dietary pattern was based on substantial carbohydrate restriction aimed at sustaining nutritional ketosis, together with a moderate protein intake and predominance of dietary fat as the main energy source. Total estimated caloric intake was approximately 2,400 kcal/day, distributed as 150 g/day of protein (600 kcal; ≈25% of total energy intake), less than 20 g/day of carbohydrates derived from vegetables (≈80 kcal; <5% of total energy intake), and fat consumed to satiety as the principal macronutrient for energy provision (≈1,680 kcal; ≈70% of total energy intake). Dietary fat sources included both saturated and polyunsaturated fats (meat from various animal sources, fish, cheese, coconut oil, butter, Serrano ham, chorizo, and avocado) and monounsaturated fat, mainly olive oil.

This macronutrient distribution remained consistent with a classic ketogenic dietary pattern throughout the observation period. Protein intake was adjusted according to concurrent physical activity: following the introduction of resistance training in January 2025, protein intake was calculated at 2 g/kg body weight/day, provided entirely through whole foods without protein supplementation. No prolonged interruptions of the KD or significant reintroductions of carbohydrates were reported during the study period.

2.3 Variables assessed

2.3.1 Hematological parameters

Red blood cell count, hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), total leukocyte count, leukocyte differential, platelet count, and mean platelet volume (MPV) were analyzed.

2.3.2 Lipid profile

Serum concentrations of total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides, and apolipoprotein B (when available) were determined.

2.3.3 Liver function

Alanine aminotransferase (ALT/GPT), aspartate aminotransferase (AST/GOT), gamma-glutamyl transferase (GGT), alkaline phosphatase, and total bilirubin were evaluated.

2.3.4 Glucose metabolism

Serum glucose, glycated hemoglobin (HbA1c), and fasting insulin were assessed.

2.3.5 Renal function and electrolyte balance

Urea, serum creatinine, estimated glomerular filtration rate (CKD-EPI and MDRD-4), sodium, potassium, chloride, corrected calcium, phosphorus, magnesium, and serum osmolality were recorded.

2.3.6 Iron metabolism

Serum iron, transferrin, ferritin, total iron-binding capacity, and transferrin saturation index were evaluated.

2.3.7 Hormonal, vitamin, and inflammatory profile

Thyroid-stimulating hormone (TSH), free thyroxine (FT4), total testosterone, free testosterone, basal cortisol, vitamin B12, folate, vitamin D, and C-reactive protein (CRP) were analyzed.

2.3.8 Ketone monitoring

Nutritional ketosis was objectively monitored throughout the follow-up period using the AccuGence Multi-Monitoring

System (Model PM900), a point-of-care device that quantifies capillary blood β-hydroxybutyrate (BHB) concentration via enzymatic reactive strips, expressed in mmol/L. Measurements were performed three times per week throughout the 28-month follow-up period, providing direct biochemical confirmation of sustained ketogenic adherence, complementary to the self-reported and weighed dietary macronutrient distribution.

2.3.9 Body composition assessment

Segmental multifrequency bioelectrical impedance analysis (TANITA MC 780-MA) was performed once, at the final clinical evaluation in May 2026 (28 months after diet initiation), providing height, weight, body mass index (BMI), fat mass percentage, skeletal muscle mass, visceral fat index, and intracellular hydration status.

2.4 Procedures

All laboratory analyses were performed in accredited clinical laboratories using standardized automated methods with internal quality control. Results were obtained from venous blood samples collected after overnight fasting. LDL cholesterol was calculated (not directly measured) at all timepoints. The dates and laboratory-specific reference ranges are reported in **Table 1** and **Table 2**. Reference values used to interpret results corresponded to the ranges established by each participating laboratory and are reported explicitly alongside each measurement.

2.5 Ethical considerations and informed consent

This case report was conducted in accordance with the ethical principles of the Declaration of Helsinki of the World Medical Association and its subsequent amendments. The patient received comprehensive information about the objectives, methods, assessment procedures, and intended use of data obtained during his routine clinical follow-up, and provided written informed consent for the use of these data in the preparation and publication of the case report. Patient data were handled confidentially, and the case was anonymized in accordance with current data protection regulations. Because this was a retrospective observational single-case study based on laboratory results obtained in routine clinical practice, no additional interventions were performed and the participant's clinical management was not modified.

2.6 Statistical analysis

Given the descriptive nature of the study and the single-case design, results were analyzed through direct comparison of serial laboratory assessments over time, without the use of formal statistical tests, identifying clinically relevant variations in lipid profile, liver function, and metabolic parameters over the follow-up period.

3. RESULTS AND DISCUSSION

3.1 Results

During the 28-month follow-up, marked variability was observed in the lipid profile, whereas most hematological, glycemic, hormonal, and renal parameters remained within reference ranges at the timepoints assessed. A transient elevation of liver enzymes was detected in January 2026, with subsequent resolution.

3.1.1 Lipid profile

Table 1 shows the evolution of the main lipid markers during the study period. LDL cholesterol fluctuated markedly, rather than remaining persistently elevated, ranging from 137.4 mg/dL (January 2026) to 295.8 mg/dL (April 2025). Triglycerides remained consistently low (23–99 mg/dL) at all timepoints, and HDL cholesterol remained within a generally favorable range (44–76.2 mg/dL) but never reached the ≥80 mg/dL threshold formally required for the LMHR phenotype, including at the earliest available measurement (44 mg/dL, June 2024, approximately five months after diet initiation).

Table 1. Longitudinal evolution of the lipid profile

Parameter	Jun 2024	Apr 2025	Jan 2026	May 2026 (A)	May 2026 (B)
Total cholesterol (mg/dL)	—	382	194	307	343
LDL cholesterol (mg/dL)	271	295.8	137.4	221.4	257
HDL cholesterol (mg/dL)	44	73	52	68	76.2
Triglycerides (mg/dL)	99	66	23	88	50
ApoB (mg/dL)	—	—	92	—	—

Note. Longitudinal evolution of the lipid profile in an adult without known metabolic disease during 28 months of KD adherence (diet initiated January 2024), illustrating marked intra-individual LDL-C variability rather than persistent elevation, alongside consistently low triglycerides and a generally favorable, though never formally elevated (≥80 mg/dL), HDL-C. LDL-C was calculated at all timepoints. The Eurofins (B) assessment (20 May 2026) was performed one day after the hospital-based (A) assessment (19 May 2026).

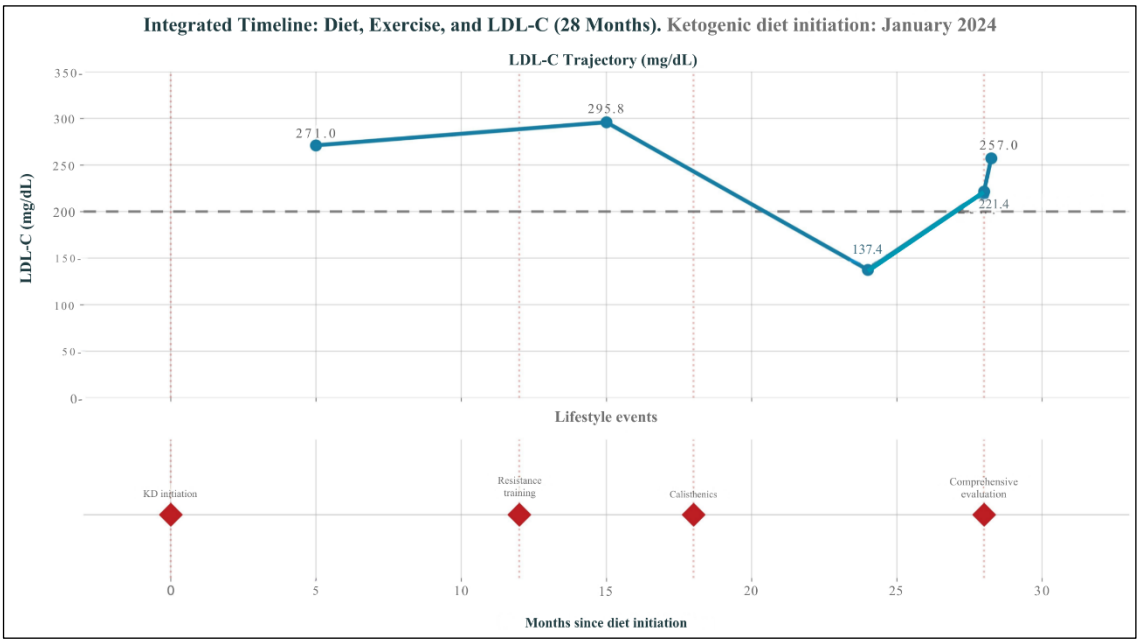

Fig. 1. Integrated timeline of dietary intervention, lifestyle modifications, and LDL-C evolution over 28 months of follow-up.

3.1.2 Liver function

The evolution of liver function markers is presented in **Table 2**.

Table 2. Longitudinal evolution of liver function parameters

Parameter	Apr 2025	Jan 2026	May 2026 (A)	May 2026 (B)
AST/GOT (U/L)	23	74	22	—
ALT/GPT (U/L)	54	132	62	42
GGT (U/L)	21	31	17	14
Alkaline phosphatase (U/L)	73	64	85	—
Total bilirubin (mg/dL)	0.50	0.37	0.55	—

Note. Longitudinal evolution of liver function parameters, showing a transient increase in transaminases in January 2026 with subsequent resolution (ALT 42 U/L in the Eurofins assessment of 20 May 2026) and stable values for other hepatic markers.

In January 2026, elevations in AST and ALT were observed, reaching 74 U/L and 132 U/L, respectively. In the assessments performed four months later, ALT decreased to within the reference interval (62 U/L, hospital (A); 42 U/L, Eurofins (B)). GGT and the remaining liver markers remained within normal ranges throughout follow-up. Several unverified factors could have contributed to the January 2026 elevation, including vigorous physical exercise prior to sample collection, transient dietary change, minor illness, or supplement use; none of these were systematically documented, and this transient finding should not be attributed to ketogenic-diet adaptation without direct supporting evidence.

3.1.3 Glucose metabolism and renal function

Serum glucose ranged from 92 to 99 mg/dL across the timepoints measured. Glycated hemoglobin was measured only once, in April 2025 (5.4%), and should not be interpreted as a longitudinally stable finding.

Serum creatinine remained between 0.60 and 0.88 mg/dL, and estimated glomerular filtration rate was above 90 mL/min/1.73 m² in all assessments. Blood urea showed a slight elevation in May 2026 (57 mg/dL), and potassium presented mild elevations in April 2025 (5.4 mmol/L) and May 2026 (5.1 mmol/L). These mild elevations in urea and potassium are noted explicitly, as they represent a deviation from strict reference-range stability; they may warrant brief clinical consideration in the context of a high-protein, high-fat dietary pattern, without implying a specific causal mechanism.

3.1.4 Hematological parameters

Hematological values remained within reference ranges at all assessed timepoints. Hemoglobin varied between 13.7 and 15.2 g/dL, leukocytes between 4.77 and 5.56 $\times 10^3/\mu L$, and platelets between 189 and 203 $\times 10^3/\mu L$. No findings compatible with anemia, leukocytosis, leukopenia, or thrombocytopenia were observed.

3.1.5 Hormonal, vitamin, and inflammatory profile

TSH was measured on three occasions (April 2025, January 2026, May 2026), ranging from 1.59 to 3.00 µUI/mL. Free thyroxine was measured only once (May 2026): 17.85 pmol/L. Total testosterone was measured on three occasions, ranging between 7.25 and 7.64 ng/mL; free testosterone was measured only once (May 2026): 25.2 pg/mL. Vitamin D was measured on three occasions, ranging from 29.0 to 36.1 ng/mL, and vitamin B12 remained within reference values at all assessed timepoints. C-reactive protein (CRP) was measured on three occasions (April 2025: 0.07 mg/dL; January 2026: 0.11 mg/dL; May 2026, (A): 0.07 mg/dL) and was not reported in the Eurofins assessment; all available values were within the normal range. Fasting insulin was measured only once (May 2026: 3.80 µUI/mL) and should not be described as stable across follow-up.

3.1.6 Dietary quantification

Daily food weighing confirmed sustained adherence to a classic ketogenic macronutrient distribution throughout the 28-month follow-up period, with an estimated total caloric intake of approximately 2,400 kcal/day (≈70% fat, ≈25% protein, <5% carbohydrate). Protein intake was proportionally increased from month 12 onward (2 g/kg body weight/day) to accompany the introduction of resistance training, without recourse to protein supplementation.

3.1.7 Ketone monitoring

Capillary blood BHB concentrations, measured three times weekly with the AccuGence PM900 device, ranged between 0.5 and 2.3 mmol/L throughout the entire 28-month follow-up period, confirming sustained nutritional ketosis of light-to-moderate intensity and providing objective biochemical support for the reported dietary adherence, beyond self-report alone.

3.1.8 Body composition

At the final assessment (May 2026, month 28), bioelectrical impedance analysis showed a body composition compatible with an athletic phenotype, characterized by elevated skeletal muscle mass, low body fat percentage (11.1%), reduced visceral fat index, and adequate intracellular hydration. Because this assessment was performed only once, at the study endpoint, it is not possible to determine whether body composition changed meaningfully across the earlier phases of dietary and exercise intervention described.

3.1.9 Overall findings

The main changes observed during follow-up involved marked intra-individual LDL-C and total cholesterol fluctuation, accompanied by consistently low triglycerides and a generally favorable, though never formally elevated, HDL-C. Glycemic, hematological, renal, hormonal, and inflammatory markers remained within reference intervals at the timepoints assessed, although several of these parameters were measured only once and should not be described as longitudinally stable. The transient elevation in transaminases recorded in January 2026 resolved in subsequent assessments.

3.2 Discussion

The findings of this case report reveal a distinctive evolution of the lipid profile in a young adult without known metabolic disease, characterized by markedly fluctuating LDL cholesterol concentrations accompanied by low triglycerides, generally favorable HDL cholesterol, normoglycemia at the timepoints assessed, low inflammatory markers, and absence of relevant endocrine-metabolic disturbances. This pattern differs from that commonly observed in individuals with metabolic syndrome, obesity, or insulin resistance, in whom hypertriglyceridemia, reduced HDL-C, and chronic inflammation typically coexist with elevated LDL cholesterol (Grundy, 2016).

Traditional interpretation of LDL-C concentrations above 190 mg/dL is based on decades of epidemiological, genetic, and clinical evidence linking atherogenic lipoproteins causally to the development of atherosclerosis (Mach et al., 2020). Among specific metabolic subgroups that do not appear to fit fully within this classic model, the lean mass hyper-responder (LMHR) phenotype has been described in normal-weight or lean individuals following low-carbohydrate or KDs, formally defined by three concurrent cut points: LDL-C ≥200 mg/dL, HDL-C ≥80 mg/dL, and triglycerides ≤70 mg/dL (Norwitz et al., 2022a). These thresholds were deliberately selected as statistically rare in the general population, such that meeting all three simultaneously would be highly unlikely by chance alone; the strictness of this triad is therefore central to the definition, rather than an incidental feature.

The data observed in the present case show partial overlap with this phenotype but do not fully satisfy its formal criteria. While triglycerides remained consistently low throughout follow-up (23–99 mg/dL) and LDL-C reached markedly elevated concentrations (137.4–295.8 mg/dL), HDL-C—despite remaining within a generally favorable range (44–76.2 mg/dL)—never reached the ≥80 mg/dL threshold required for strict LMHR classification, including at the earliest available measurement (44 mg/dL, June 2024). Accordingly, we describe this case as exhibiting an LMHR-like lipid pattern rather than a confirmed LMHR phenotype. This distinction is clinically relevant: because the LMHR construct integrates simultaneous thresholds across three parameters specifically to isolate a rare and reproducible metabolic subgroup, extrapolating findings from LMHR cohort studies, including meta-analytic evidence that LDL-C increases on low-carbohydrate diets are largely confined to individuals with normal (not high) body weight (Soto-Mota et al., 2024), to individuals who meet only two of the three criteria should be done cautiously.

Norwitz and colleagues proposed the lipid energy model, according to which extreme LDL-C elevations observed in some individuals on very low-carbohydrate diets may represent a physiological adaptation to increased energy transport mediated by lipoproteins, particularly in lean and physically active subjects (Norwitz et al., 2021). According to this hypothesis, continuous mobilization of fatty acids from adipose tissue increases VLDL particle turnover and, secondarily, circulating LDL concentrations.

The temporal relationship between lifestyle modifications and LDL-C fluctuations is summarized in **Figure 1**. The initial LDL-C peak (295.8 mg/dL, April 2025) occurred approximately three months after the introduction of resistance

training and vitamin D/magnesium supplementation—that is, following rather than preceding this lifestyle change, which runs counter to a straightforward lifestyle-driven explanation of decreasing LDL-C with exercise onset. The lowest LDL-C value recorded (137.4 mg/dL, January 2026) occurred approximately six months after the addition of calisthenics, creatine monohydrate, and omega-3 supplementation, a timeframe compatible with a possible influence of these interventions. However, the subsequent increase in LDL-C observed in May 2026 (221.4–257 mg/dL) occurred approximately ten months after the last documented lifestyle change, with no additional modification recorded during this interval. This pattern should therefore be interpreted with caution: while consistent in part with the lipid energy model's proposition that energy balance and lean tissue accrual can modulate lipoprotein trafficking, the relationship is not univocally causal, and factors beyond those captured in this case report—such as unmeasured variations in caloric intake or analytical variability between laboratories—may have contributed to the observed variability.

Interestingly, the objectively confirmed range of capillary BHB concentrations observed in this case (0.5–2.3 mmol/L) suggests that the depth of nutritional ketosis was not constant throughout follow-up, but fluctuated between light and moderate ketosis. Within the lipid energy model framework, deeper or more sustained ketosis is thought to reflect greater reliance on fatty acid oxidation and hepatic VLDL/LDL particle turnover; it is therefore plausible that periods of more pronounced ketosis coincided with higher circulating LDL-C, while periods of comparatively milder ketosis coincided with its reduction. However, because BHB measurements were not time-matched to each lipid assessment in the present dataset, this potential association remains speculative and should be interpreted as a hypothesis-generating observation rather than a demonstrated mechanistic link.

The precise dietary quantification available in this case allows a more rigorous interpretation of the observed LDL-C fluctuations than is typically possible in case reports of the LMHR-like pattern. Despite a substantial and consistent intake of saturated fat sources (butter, coconut oil, cheese, and processed meats) throughout the follow-up period, LDL-C values varied markedly over time rather than remaining persistently elevated, suggesting that factors other than dietary saturated fat content—such as energy balance, lean tissue accrual, and training status—may have played a more prominent role in modulating lipoprotein concentrations, consistent with the lipid energy model (Norwitz et al., 2021; Norwitz & Loh, 2020).

An earlier cross-sectional study by Budoff et al. (2024), comparing coronary computed tomography angiography findings between LMHR individuals with markedly elevated LDL-C (mean 254 mg/dL) and matched controls with substantially lower LDL-C (mean 123 mg/dL), found no significant difference in coronary plaque burden between groups, nor any correlation between LDL-C and plaque score. A subsequent longitudinal analysis by the same research group, which reported that baseline plaque—rather than ApoB or cumulative LDL-C exposure—predicted plaque progression, was retracted in 2026 due to methodological concerns regarding selective outcome reporting and should not be relied upon as supporting evidence. Consequently, the only currently valid evidence from this research line is the original cross-sectional comparison, which is hypothesis-generating rather than conclusive, given its observational design and relatively short follow-up duration (Budoff et al., 2024).

Cardiovascular risk does not depend exclusively on LDL cholesterol concentration but also on other factors such as systemic inflammation, insulin resistance, hypertension, smoking, and accumulated atherosclerotic burden (Libby, 2021). In the present case, the available CRP measurements were within the normal range at all assessed timepoints, which may indicate a generally favorable inflammatory profile, although this should be interpreted with the caveat that CRP was not available at every laboratory assessment.

Some studies in older populations have reported an absent or inverse association between total cholesterol and all-cause mortality (Ravnskov et al., 2016; Weverling-Rijnsburger et al., 1997), and elevated cholesterol has been observed among centenarians with preserved functional status (Barzilai et al., 2003; Hu et al., 2024). However, these findings are drawn from elderly cohorts and are particularly susceptible to survivor bias and reverse causality; their applicability to a 34-year-old adult with severe LDL-C elevation is therefore indirect and should not be overstated.

Regarding the origin of the hypercholesterolemia observed in this case, the available data do not allow confirmation or exclusion of familial hypercholesterolemia. A diet-associated rise and an inherited predisposition are not mutually exclusive, and the absence of documented pre-diet LDL-C, family history assessment, and genetic testing precludes any definitive conclusion regarding etiology. The marked fluctuation observed is not readily explained by a fixed monogenic alteration alone, although familial hypercholesterolemia cannot be formally excluded without genetic testing or family history assessment. Recent studies have shown that some individuals experience increases of more than 100 mg/dL in LDL-C after adopting ketogenic or very low-carbohydrate diets, a phenomenon that partially or completely reverses upon carbohydrate reintroduction or adjustment of energy balance (Norwitz & Loh, 2020).

Nonetheless, these findings must be interpreted cautiously. Major scientific societies continue to consider LDL cholesterol a causal factor in atherosclerosis and recommend interventions aimed at reducing its concentration when levels are persistently elevated (Ference et al., 2017). The 2025 Focused Update of the ESC/EAS dyslipidaemia guidelines reaffirms the LDL-C treatment targets established in 2019, while refining cardiovascular risk stratification through the SCORE2/SCORE2-OP algorithms and incorporating new risk modifiers such as elevated lipoprotein(a) and coronary artery calcium score (ESC/EAS, 2025). This reinforces that, despite emerging evidence on phenotype-specific lipid patterns such as LMHR, current clinical guidance does not support withholding risk stratification or treatment consideration based solely on a favorable metabolic profile. Current evidence on LMHR-like patterns and KDs remains emergent and is based mainly on observational studies and case series; it is therefore not possible to conclude that very high LDL-C concentrations are harmless in the long term, even in individuals with an otherwise favorable metabolic profile.

Strengths of this case include the availability of multiple laboratory determinations over more than two years of follow-

up, objective ketone monitoring, detailed dietary quantification, and an anthropometric assessment. However, several limitations should be acknowledged. First, no pre-diet lipid baseline was available, precluding any causal attribution of the observed hypercholesterolemia to the KD. Second, segmental bioelectrical impedance analysis was performed only once, at the final assessment (May 2026), rather than at each laboratory time point; body composition data are therefore available only for the endpoint of follow-up. Third, ApoB was measured on a single occasion (January 2026), coinciding with the nadir of LDL-C observed during follow-up, and was not available at the time points corresponding to peak LDL-C concentrations (April 2025 and May 2026); consequently, this case report cannot determine whether the extreme LDL-C elevations reflected a proportional increase in LDL particle number or predominantly larger, less atherogenic particles, a distinction central to the LMHR phenotype characterization. Fourth, CRP was not available for the Eurofins assessment reporting the highest LDL-C value (257 mg/dL, May 2026). Fifth, the two May 2026 LDL-C values (221.4 vs. 257 mg/dL) were obtained from different laboratories one day apart, and possible inter-laboratory analytical variability cannot be excluded as a contributor to this difference. Finally, the single-case nature of the study, the absence of genetic testing, and the absence of vascular imaging (e.g., coronary computed tomography angiography or carotid ultrasound) represent additional limitations that preclude generalization or definitive characterization of atherosclerotic risk. Future studies of this phenotype should prioritize a documented pre-diet baseline, concurrent ApoB and CRP measurement at every lipid assessment, and longitudinal body composition tracking.

Overall, the results suggest that clinical interpretation of fluctuating LDL cholesterol concentrations may require a broader assessment of individual metabolic context, dietary intake, and lifestyle factors over time. The coexistence of markedly variable LDL-C with low triglycerides, generally favorable HDL-C, normoglycemia at the timepoints assessed, and low inflammatory markers represents a biological scenario that remains the subject of active scientific debate and requires long-term prospective studies with complete concurrent biomarker panels to establish its true impact on cardiovascular health.

4. CONCLUSION

This longitudinal case report demonstrates marked intra-individual LDL-C variability during approximately 28 months of ketogenic-diet adherence in an adult without known metabolic disease, accompanied by consistently low triglycerides, generally favorable HDL cholesterol, normoglycemia at the timepoints assessed, low inflammatory markers, and absence of significant endocrine-metabolic abnormalities. Over the observation period, LDL-C fluctuated by more than 150 mg/dL between its lowest and highest recorded values, without a clear, fully documented explanatory pattern of lifestyle change across the entire follow-up period.

The findings are consistent with features recently described in individuals with an LMHR-like lipid pattern, an emerging area of interest associated with low-carbohydrate dietary patterns and a favorable metabolic profile, although the present case did not meet the strict HDL-C threshold required for formal LMHR classification. This distinction underscores that intermediate or partial phenotypes may be more common in clinical practice than the narrowly defined LMHR construct, and that current evidence is insufficient to determine whether such intermediate patterns confer cardiovascular risk comparable to, lower than, or equivalent to formally classified LMHR or traditional hypercholesterolemia.

The coexistence of very high LDL cholesterol concentrations with favorable metabolic markers highlights the need for comprehensive clinical assessment that considers not only atherogenic lipoproteins but also other determinants of metabolic and cardiovascular health, such as inflammation, oxidative stress, and glucose regulation.

Given the single-case nature of the present study, the absence of a pre-diet baseline, and the incomplete concurrent availability of ApoB and CRP at peak LDL-C values, the results cannot be generalized and do not establish causality, phenotype confirmation, or cardiovascular safety. Nevertheless, they provide descriptive, hypothesis-generating evidence regarding a metabolic pattern that is currently the subject of scientific debate and underscore the need for long-term prospective studies incorporating complete concurrent biomarker panels and vascular imaging techniques to clarify the clinical significance of extreme LDL-C fluctuations in adults without known metabolic disease.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest, whether financial, personal, commercial, or academic, that could have influenced the design, conduct, analysis, interpretation, or publication of this case report. None of the authors received honoraria, grants, royalties, or any other form of compensation from pharmaceutical companies, nutritional supplement manufacturers, body composition technology providers, or any other entity with interests related to the content of this work.

FUNDING

This work received no external funding. The costs associated with clinical evaluation, laboratory determinations, and the single body composition analysis performed at the end of follow-up were fully covered by the patient as part of his routine nutritional care. The authors did not receive any financial remuneration for the preparation of this case report.

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